distinguished at the primary structural level (i.e., sequence) and at the secondary and tertiary structural levels.

Based on the foregoing, applicants request rejoinder of claims 1-21 and 27.

Priority

The Examiner has acknowledged receipt of the papers submitted under 35 U.S.C 119(a)-(d). The Examiner indicates that the papers have been placed of record in the file.

Information Disclosure Statement

The Examiner has acknowledged that he has considered and made of record the references submitted with the Information Disclosure Statements filed on August 24, 2006, June 1, 2007, and July 21, 2008 as indicated on the PTO Forms 1449 included with the October 10, 2008 Office Action.

Specification

In the October 10, 2008 Office Action, the Examiner indicated that the proprietary nature of trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

In response, applicants have hereinabove amended the specification to identify trademarks in uppercase and to provide a generic description of the product identified by the trademark where necessary. Applicants maintain that the amendments to the specification add no new matter.

Claim Objection

Claim 6 is objected to as being dependent on a withdrawn claim (claim 1). Applicants have amended claim 6 to delete reference to claim 1 and to incorporate all of the structural limitations of claim 1, thereby overcoming this objection.

Claim Rejections - 35 U.S.C §112

The Examiner has alleged that the specification provides insufficient written description of the subject matter of claim 15. The Examiner's objection appears to be based on his opinion that the specification provides insufficient guidance as to specific variants and fragments of the claimed sequences that will have the antibacterial and/or antifungal activity required by the claims, and provides no description of polynucleotides that hybridize to those claimed and encodes a peptide having the requisite activity. The Examiner also alleges that the specification only provides a sufficient structure of the chemical structure of the peptides set forth in SEQ ID NOs: 1, 4 and 9.

Applicants understand that this rejection will apply to all claims pending in the application as a result of this amendment and the introduction of the requirement that the claimed polynucleotides encode peptides having antibacterial and/or antifungal activity.

Applicants have deleted language in the claims directed to hybridization under high stringency conditions, rendering this aspect of the rejection moot.

Applicants traverse the Examiner's rejection.

Applicants submit that the present specification provides detailed information and, as a consequence, satisfies the written description

requirement. For example, the specification provides the sequence of the elected peptide (SEQ ID NO: 4) and its precursor (SEQ ID NO: 1) and polynucleotides encoding SEQ ID NO: 1 and SEQ ID NO: 4 and an allelic variant thereof. Furthermore, the specification provides the sequence of *three (3)* additional *G. mellonella* related peptides and encoding polynucleotides, which share between 42% and 89% identity at the amino acid level and 57% and 90% identity at the nucleotide level. Accordingly, the specification describes a class of peptides having a lower degree of sequence identify than that required by the claims. The skilled artisan will be readily able to predict additional sequences using current computer technology (as taught in the USPTO's Training Manual).

Furthermore, the specification discusses the various structural elements of the peptides that are important for biological activity. For example, at page 42, the specification describes the moricin peptides as comprising a helical structure comprising hydrophobic residues at the C terminal end of the helix and an amphipathic region comprising basic amino acids at the N-terminal end of the helix and a C-terminus comprising charged amino acids.

The specification also provides a consensus sequence of the claimed *G. mellonella* moricin peptides based on the variety of distinct peptides isolated by the inventors (SEQ ID NO: 62), which clearly indicates sites at which substitutions can be made, and which substitution can be made. As discussed in the Training Materials, whilst not all of the recited substitutions may result in a peptide having the requisite activity, based on the teachings in the specification those of ordinary skill in the art would expect that many of these substitutions would result in a protein having the required activity.

Accordingly, following the Training Materials set out by the USPTO, the specification provides the sequence of several peptides

structurally related at the tertiary level (i.e., more than the one actually required), identifies structural regions that are important for biological activity and further identifies specific sites at which amino acid residues can be substituted while retaining biological activity. Accordingly, the specification satisfies the USPTO's guidelines as to the requirements of written description, and applicants request that the Examiner reconsider and withdrawal this rejection.

Enablement

The Examiner also alleges that claims 6, 8-10, 13 and 15 are not enabled. Applicants reading of the Office Action indicates that the Examiner's rejection is based on the following reasoning:

(i) most claims do not require that the claimed peptides have antibacterial and/or antifungal activity;

(ii) the claims encompass any polynucleotide or polypeptide that comprises two residues of the recited sequences;

(iii) the specification only discloses SEQ ID NO: 4 and its encoding polynucleotides and does not disclose sequences having 66% identity thereto having antibacterial and/or antifungal activity and that it is not possible to predict where suitable substitutions can be made (e.g., using computational processes);

(iv) the specification does not disclose any sequences that hybridize under highly stringent conditions to the recited sequence and encode a peptide having antibacterial and/or antifungal activity; and

(v) the production of transgenic animals is highly unpredictable.

Applicants have cancelled language in the claims requiring hybridization under highly stringent conditions, rendering this aspect of the rejection moot.

Applicants have also amended all claims to require that the claimed peptides (including biologically active fragments thereof) have antibacterial and/or antifungal activity.

Notwithstanding that applicants maintain that it was clear that the claims as filed encompassed only biologically active fragments of the recited peptides by virtue of clause ix), applicants have in this amendment clarified that this is true. The term biologically active is defined in the specification as maintaining the biological activity of the full length peptide, in this case antibacterial and/or antifungal activity as required by the claims. Accordingly, the claims do not encompass any fragment of the recited sequences including fragments of only two amino acids, since those fragments would not have the requisite biological activity.

In contrast to the Examiner's allegation that the specification only enables SEQ ID NO: 4 and its encoding polynucleotides and not sequences having a degree of % identity thereto, applicants submit that the specification clearly discloses a variety of peptides related at the secondary and/or tertiary level which share between 42% and 89% identity at the amino acid level. The specification also demonstrates that these peptides have antibacterial and/or antifungal activity. Accordingly, the specification enables production of peptides having far less identity than the 80% recited in the claims as amended.

Furthermore, as discussed in detail above, the specification clearly teaches a consensus sequence that shows which amino acids may be substituted, or which amino acids may be omitted (e.g., in a fragment), see SEQ ID NO: 62. This consensus sequence was not based on computational predictions as the Examiner appears to believe, but on the sequence of peptides actually shown to have the requisite activity. Furthermore, the specification teaches the desired secondary/tertiary structure of a peptide of the invention and the

residues involved in attaining that structure, e.g., at page 42. Based on the teaching in SEQ ID NO: 62 and/or the teaching at page 42, the skilled artisan would readily be able to determine peptides having antibacterial and/or antifungal activity. The skilled artisan would also be able to assess the activity of those peptides using methods exemplified in the instant application, e.g., at page 31, lines 21 to 32.

As for the Examiner's allegation that the production of transgenic non-human animals is unpredictable, applicants respectfully traverse. The citations relied upon by the Examiner in attempting to establish that production of transgenic animals is unpredictable merely establishes that the genetic background of the transgenic organism (e.g., an inbred mouse) effects the phenotypic effect of the transgene. One of these references (Brampton *et al., Brain Res. 841*: 123-134, 1999) does not even actually produce transgenic animals, instead performing experiments on unmodified inbred mice.

Techniques for producing transgenic animals have been in use for over 20 years (e.g., pronuclear microinjection-based methods), and are now standard practice. Applicants submit Rülicke and Hübscher *Exp. Physiol 85 (6):* 589 (2000), which clearly teaches that whilst the frequency of transgenic founders produced using art recognized methods may vary between species, it "is efficient enough to render this technique applicable to a wide range of mammals" (see Abstract).

Applicants request that the Examiner reconsider and withdraw his rejection in view of the foregoing comments.

Clarity

The Examiner has also rejected claims 6, 8-10 and 15 as being indefinite as a result of the term "high stringency conditions".

This term has been deleted from the claims thereby rendering this objection moot.

Novelty

The Examiner alleges that claims 6, 8-10, 13 and 15 lack novelty over the disclosure in WO 02/086072 (Altier et al) of a polynucleotide with 3 consecutive nucleotides in common with SEQ ID NO: 9 and three consecutive amino acids in common with SEQ ID NO: 4.

As discussed above, applicants have amended the claims to clarify that the fragments defined are biologically active (i.e., the fragment itself must have antibacterial and/or antifungal activity). The 3 amino acid region of the peptide disclosed in Altier et al that is homologous to a region of a peptide disclosed in the instant application could not have the antibacterial and/or antifungal activity required by the claims as amended (i.e., it could not form the secondary/tertiary structure required to exert such biological activity). Nor does Altier disclose a peptide or polynucleotide having 80% identity to a sequence recited in the present claims. Accordingly Altier does not disclose a peptide or a *biologically active* fragment thereof or polynucleotide encoding same as required by the claims of the instant application, and all claims are novel over this disclosure.

Supplemental Information Disclosure Statement

In accordance with their duty of disclosure under 37 C.F.R. §1.56, applicants direct the Examiner's attention to the following document listed below which is also listed on the Form PTO-1449 (Substitute) attached hereto as **(Exhibit A)**.

This Supplemental Information Disclosure Statement is being submitted pursuant to 37 C.F.R. §1.97 (c)(2) before the mailing of a final office action. Pursuant to C.F.R. §1.17(p) the fee for filing this Supplemental Information Disclosure Statement is $180.00.

A copy of item 1 is attached hereto as **Exhibit 1**.

Applicants request that the document listed below and on the Form PTO-1449 (Substitute) be considered and made of record in the above-identified application.

1. Rülicke, T. and Hübscher, U., "Germ line transformation of mammals by pronuclear microinjection," *Experimental Physiology* (2000) 85(6), 589-601 **(Exhibit 1)**.

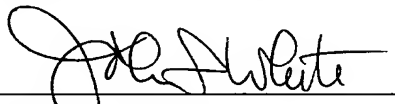
Conclusion

Applicants respectfully submit that all grounds of rejection set forth in the October 10, 2008 Office Action have been overcome. Applicants therefore respectfully request that the Examiner reconsider and withdraw these grounds of rejection, and earnestly solicit allowance of all claims pending in the subject application.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

No fee is deemed necessary in connection with the filing of this Substitute Amendment. However, if any fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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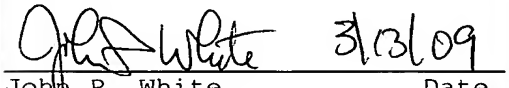
I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450



John P. White Date
Reg. No. 28,678

EXHIBIT A